ACRIN Experience with Quantitative PET

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ACRIN Background

- NCI funded collaborative group with a mission to perform multicenter trials of imaging
- Originally funded in 1999
- Accrued over 75,000 patients in over 25 trials at over 100 sites
- Trials of image detection, characterization, therapeutic guidance, monitoring (including clinical outcomes)
- Trials including multiple modalities: CT, MR, PET, SPECT, Mammography, and Ultrasound
<table>
<thead>
<tr>
<th>Study #</th>
<th>Target</th>
<th>Agent</th>
<th>Status</th>
<th>Accrual</th>
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<tbody>
<tr>
<td>6665</td>
<td>GIST</td>
<td>FDG</td>
<td>Follow up</td>
<td>63</td>
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<td>NSCLCA</td>
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<td>H &amp; N</td>
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<td>*6687</td>
<td>Prostate (bone)</td>
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<td>Open</td>
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<td>*6688</td>
<td>Breast</td>
<td>FLT</td>
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<td>*6689</td>
<td>Glioma</td>
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<td>Alzheimer’s</td>
<td>PIB, FPIB, AV45</td>
<td>Open</td>
<td>31</td>
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</table>

*Performed under NCI sponsored IND
Lessons Learned

- Quality Control
  - Qualification
  - Ongoing Quality Control
- Accrual
  - Site recruitment
- Trial Design/Qualification Strategy
ACRIN Site Qualification

- Establish Site Infrastructure
  - ACR accreditation or demonstration of proper technology/personnel (Only complete ring dedicated PET scanners)
- Uniform Phantom Images
- 2 Sample Clinical Images using ACRIN acquisition Protocol

148 sites have been qualified
<table>
<thead>
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<tbody>
<tr>
<td>Overanonymization of DICOM header</td>
<td>0 (0)</td>
<td>4 (0)</td>
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<tr>
<td>Incorrect information in DICOM header/on application</td>
<td>15 (1)</td>
<td>10 (0)</td>
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<td>Clock synchronization problem</td>
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<td>Incomplete application</td>
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<td>Improper data format</td>
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<td>1 (0)</td>
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<td>Image display problem</td>
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<td>Normalization calibration</td>
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<td>SUV calibration</td>
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<td>Total</td>
<td>36 (4)</td>
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*Scheuermann et al J Nucl Med. 2009 Jul;50(7):1187-93*
Typical Calibration Problem
Categories of Failures

- Some information in the DICOM header needs to be edited
  - Incorrect weight for a phantom
  - Typo while entering weight, dose, or dose assay time
  - Failing to compensate for time difference between dose calibrator and scanner
  - Failing to account for residual activity in syringe

- New data must be acquired and submitted to ACRIN
  - Uncertainty about the time or amount of injection
  - Failure to record and account for residual activity in syringe

- Some or all of the calibrations on the scanner must be redone and new application submitted to ACRIN
Image and header review to assess protocol compliance, with timely intervention to correct problems at individual sites

Protocol-specific image quality control

- Ongoing monitoring of instrument performance
- Site and core-laboratory radiologist review of submitted images
- Quantitative assessments (e.g., reference-tissue SUV)

Typically greater than 90% acceptable data quality

- Most common problem is imaging out-time window
Analysis

\[
\text{SUV} = \frac{\text{tissue conc. (µCi/gm)}}{\text{inj. dose (µCi)/body weight (gm)}}
\]

\[
\text{SUV}_{\text{max}} = \text{Maximum SUV within the ROI (tumor)}
\]
- Single voxel
- Automated process

\[
\text{SUV}_{\text{peak}} = \text{Mean SUV in 0.75-1.5 cm (ideally 1.0 cm)}
\]
- diameter ROI “centered” on \(\text{SUV}_{\text{max}}\)
- Partially manual, partially automated process
Determining the SUV_{peak}

- Read the average SUV within the circular 0.75-1.5 cm ROI.

\[
\text{SUV}_{\text{peak}} = 9.55
\]
Pre-treatment Primary Tumor

Correlation between Local and Central SUV’s

Pearson correlation = 0.626
Concordance correlation = 0.611

Discordance (> 3.0 points)
14/56 = 25%

Imaging Core Laboratory
The average core lab standard deviation between readers for measurement of the Peak SUV was .5 units.
The average core lab standard deviation between readers for measurement of the percent response was 7% for peak SUV.
Primary PET Biomarker Imaging Trials: Unique Accrual Issues

• No immediate patient benefit
• Radiation Concerns
• Scheduling issues
• Site recruitment
  ▪ The “Venn Diagram” problem
Site Recruitment

Imaging Trial Sites

Therapy Trial Sites

Imaging Core Laboratory
Approach

- Focus on critical data points to minimize exposure and facilitate scheduling
- Enlarge each Cell of the Venn Diagram
  - Plan study with as liberal treatment options as possible consistent with the mechanism of the marker tested
  - Balance technical requirements on the imaging sites consistent with study needs
- Enlarge the “Union”
  - Focus on sites with clinical / imaging integration
  - Mandate the imaging component in treatment trial
Lessons

- High quality data quantitative data can be acquired in the setting of multicenter trials
- Site training is key to establishing and maintaining quality
- Accrual into PET biomarker trials is uniquely challenging